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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	

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15

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/966,746	ZAUDERER, MAURICE	
	Examin r	Art Unit	
	Zachariah Lucas	1648	

-- Th MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 1-7 are pending and under consideration in the present application. Claims 1-23 were rejected in the action mailed on July 3, 2002 (the prior action). Claims 1 and 2 were amended, and claims 8-23 were cancelled, in the response filed December 3, 2002 (Amend. A).

2. Because this action raises new grounds of rejection, it is being made Non-Final.

Information Disclosure Statement

3. The IDS filed on January 14, 2003 has been considered, and a copy attached to this action. The examiner notes that the Levinson and Wang patents on page 1, the Tanaka reference on page 13, and the PCT Search report on page 15 have been crossed out. The Levinson, Wang, and Tanaka references were crossed out as they have already been considered, and made of record, in the Form PTO 892 attached to the prior action. The PCT search report cited on page 15 is not a prior art reference, and, further, it only identifies references already made of record individually either in the present IDS, or in the prior action.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. **(Prior Rejection-Maintained)** Claims 1, 8, and 9 were rejected in the prior action under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying immunogenic gene products, does not reasonably provide enablement for a method of identifying therapeutic gene products. The claims were rejected as not enabled because determining that a compound is immunogenic does not mean that the compound may be used as a therapeutic. In order to show that a compound is therapeutic, the practitioner must run further tests to determine which of the immunogenic particles may be used to treat or inhibit the target infection. The claimed methods did not include such a step, and were therefore not enabled for screening for therapeutics.

Amend. A cancelled claims 8 and 9, and amended claim 1 to read on a method of identifying potential therapeutics for infectious diseases. The examiner does not find that the amendment avoids the rejection. A therapeutic can be any product useful for treating a disease or disorder. Such products can be those that elicit effects other than an anti-self immune response. See e.g., Levinson. Looking to the claimed method, the applicant appears to be identifying not therapeutics in general, but only those that induce such a specific anti-self response in the host cell organism. As such, what is being claimed is not a method of identifying potential therapeutics generally, but potential vaccines to the infectious diseases.

6. **(Prior Rejection- Withdrawn)** Claims 8 and 9 were rejected in the prior action under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention. These claims have been cancelled from the application. The rejection is therefore withdrawn.

7. **(New Rejection)** Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claim read on methods of screening for potential therapeutics for infectious diseases comprising the steps of 1) identifying host cell gene products that are up-regulated during infection, and 2) screening said host cell gene products for immunogenicity. For the purposes of this rejection, it is being assumed that "immunogenicity" requires that the gene products are immunogenic in the host cell organism, and that the host cell gene products that are up-regulated and immunogenic are the potential therapeutics. These claim are rejected because the applicant has not shown that the claimed method would be effective in identifying potential therapeutics for any infectious disease.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the

claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The claimed invention is towards a method of identifying potential therapeutics for infectious diseases. Both the processes according to the individual steps of the method are known in the art. See, e.g. Vournakis, and Levinson (each of which describes the use of differential expression to identify potential targets for therapeutic development); and Van Baren et al, U.S. Patent 5,879,892 (columns 1 and 2, and columns 22-23), and Boel, Immunity 2:167-175 (describing the use of gene products differentially expressed on cancer cells as epitopes capable of use to elicit CTL responses against cancer cells). However, while the prior art recognizes the value of identifying differentially expressed genes to identify potential targets of therapy against infectious diseases (Levinson), it does not teach a method of identifying differentially expressed "immunogenic" gene products with relation to infectious diseases.

In making this rejection, it is assumed that the skill of those in the art is of a high level. Also, the breadth of the claims is great. This is because the claims read on methods of identifying all gene products that may be useful as therapeutics for any infectious disease. There are a large number of pathogenic organisms that can cause infectious diseases. Further, in any one host cell-containing organism, there are a large number of potential host cell gene products that may be up-regulated by any one of these pathogenic organisms. Methods of identifying such gene products are known in the art as described above.

The presently claimed invention requires more that merely identifying differentially expressed gene products however. The applicant also claims a step in the claimed method for screening these gene products for immunogenicity, defined by the applicant as the ability to elicit

immune responses specifically against that gene product. For infectious diseases, the addition of this latter step appears to be new and not previously suggested by the art. This is because the art generally teaches that immunogenic responses, as defined by the applicant, to infectious diseases, are against not host-cell gene products, but against gene products of the infectious agent. See e.g., Blum-Tirouvanziam, J. Immunol., 154:3922-3931; and Shirai, J. Immunol., 154:2733-2742 (each disclosing viral gene products identified as capable of inducing CTL responses to fight infection). However, while a search of the prior art will show that there are host cell gene products that are up-regulated during infection (see e.g. Rosenblatt et al., Curr. Top. Microbiol. Immun., 193:25-49; and Scheuring, AIDS, 12:563-570), none of these references appear to identify any such gene products that are immunogenic in the host-cell organism. Scheuring discloses several genes that are up-regulated in host cells upon infection by HIV. Of the six genes that are identified as up-regulated in this reference, four appear to be viral in origin. Table 1, page 565. The two host cell genes that are up-regulated are intracellular in nature. There is no suggestion or indication that these intracellular host cell genes may be immunogenic.

Along with the gene products involved with intracellular processing, another set of gene products up-regulated upon infection are those involved in fighting off the infection. See e.g. Geiss et al., Virology, 266:8-16, at 12. While such gene products may be potential therapeutics against infectious diseases, and although the products may be involved in immune responses against the infection, these gene products are not themselves immunogenic. Further, these latter gene products would not generally be good targets for an immune response in any case, as targeting these proteins would likely result in a decrease in the body's ability to fight off the

infection on its own. Thus, while the art does support the identification of potential therapeutics by identifying differentially expressed genes, there is no indication in the art that any of the host cell gene products up-regulated during infection would immunogenic in that organism.

The art surrounding the claimed invention not only provides little guidance to one intending to practice the claimed method, but it also fails to provide any indication that the claimed method would be capable of identifying therapeutics for infectious diseases. Further, the specification provided in support of the claims neither provides examples of such gene products, not any guidance as to what products are likely to be effective immunogenic therapeutics against infection. Further, one skilled in the art wishing to practice the invention is faced not only by this lack of guidance in the art and the specification, but also by a large number of potential therapeutics for a large number of infectious diseases. In view of the breadth of the claims, the lack of guidance, and the lack of any indication that any therapeutics according to the claimed invention are present to be found, the examiner finds that the applicant has not provided sufficient information such that one skilled in the art would be able to practice the claimed invention without undue experimentation.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. **(Prior Rejection-Withdrawn)** Claims 1- 23 were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1, as filed, described method includes both a step of screening an identified host cell gene products for

immunogenicity, and determining which of said host cell gene products are immunogenic. It was unclear why the claim contained both these steps. In view of the amendment of claim 1, and the cancellation of claims 8-23, the rejection is withdrawn.

10. **(Prior Rejection- Withdrawn)** Claims 8 and 9 were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims have been cancelled from the application, thereby rendering the rejection moot. It is therefore withdrawn.

11. **(Prior Rejection-Withdrawn)** Claim 2 was rejected in the prior action for containing the phrase "low level in uninfected cells." The phrase is a relative term that rendered the claim indefinite. In view of the amendment made to the claim in Amend. A, the rejection is withdrawn.

12. **(New Rejection)** Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These read on a method of screening for potential therapeutics for infectious diseases comprising a step of identifying genes products that undergo increased expression upon infection, and "screening said host cell gene products for immunogenicity." This claim is rejected for indefiniteness for two reasons. First, it is unclear from the claim what is meant by "immunogenicity." Secondly, it is unclear how the method steps relate to the potential therapeutics.

In response to the prior action, the applicant indicated that the term "immunogenicity" requires that the gene product "induces an immune response which is specific against that gene product." See, Amend. A, page 6. Thus, while it is clear that immunogenicity generally requires that the gene product elicit an immune response against itself, it is unclear whether this immunogenicity may be in any organism, or if the gene product must be immunogenic in the organism in which the host cell is naturally found. In short, it is unclear from the claims whether the immunogenicity of a gene product is measured by assaying for a specific immune response against the product in the native organism of the host cell, or if the immunogenicity is measured in an organism other than the host cell native organism.

The second reason that the claims are found indefinite is that the relationship between the potential therapeutics and the immunogenic host cell gene products that are differentially expressed is unclear. It is suggested that claim 1 be amended to include language similar to the following: wherein the host cell gene products that are either up-regulated or expressed only during infection and that are found to be immunogenic are potential therapeutics for the infectious disease during which such up-regulation occurs."

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. **(Prior Rejection-Withdrawn)** Claims 1-4, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Number 5,721,351, issued to Douglas Adam Levinson (the 351 patent). Claim 1 describes a method of screening for therapeutics for infectious diseases comprising 1) identifying host cell gene products either up regulated during, or expressed only upon, infection, and 2) screening the gene products for immunogenicity. The applicant traversed this rejection on the grounds that Levinson teaches that the assays described therein include a step for the "identification of compounds exhibiting such an ability to ameliorate immune disorder symptoms." The applicant argues that this ability, and immunogenicity are not the same. According to the applicant, because the claimed method is detecting immunogenicity while the reference is seeking compounds that ameliorate immune disorder symptoms, the reference does not "inherently induce a specific immune response against the compound itself."

In view of the applicant's statement regarding the definition of "immunogenicity," the rejection is withdrawn. This is because, although it did not appear from the specification of the application that the term was read so narrowly as to include only those gene products that induce "an immune response which is specific against that gene product."

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. **(Prior Rejections-Withdrawn)** Claim 6 was rejected under 35 U.S.C. 103(a) as being unpatentable over the 351 patent in light of the teachings of U.S. Patent Number 6,004,755 (issued to Bruce Wang, and hereinafter the 158 patent) relating to the use of microarrays to identify differentially expressed genes. Claim 6 adds to claim 1 the limitation that the identification of differentially expressed genes be done using ordered microarrays.

Claim 5 was rejected under 35 U.S.C. 103(a) as being unpatentable over the 351 patent in light of U.S. Patent number 6,312,731(the 731 patent), issued to Staas et al. and U.S. Patent Number 5,846,827 (the 827 patent), issued to Celis et al. Claim 5 describes the method of claim 1 wherein the screening for immunogenicity comprises screening for a cytotoxic T-cell (CTL) response to the identified gene product.

The applicant traversed these rejections for substantially the same reasons as the 102 rejection over the 351 patent alone. The rejection is therefore withdrawn for the same reasons.

17. **(Prior Rejection- Withdrawn)** Claims 1, 2, and 3 are also rejected under 35 U.S.C. 103(a) as being obvious over the 351 patent (Levinson) and U.S. Patent Numbers 6,399,328 (the 328 patent- issued to Vournakis et al.), and 6,312,909 (the 909 patent- issued to Andrew J. Shyjan). Claim 1 and the teachings of the 351 patent are described above. Both of the other patents describe a method of identifying tumor or cancer associated gene products through differential expression. See. 328 patent, col. 4-5, and the 909 patent, col. 3, lines 58-64. Further, both of the patents also indicate that the gene products so identified may then be used to devise new treatments or yield new targets for treating cancers and tumors. 328 patent, col. 5, lines 23-31; 909 patent, col. 4, lines 10-15. Further, the references teach subtractive hybridization as

method of identifying differentially expressed genes. As such, each indicates that, having identified potential therapeutics, one skilled in the art should then assay these identified gene products for immunogenic properties.

The applicant traverses this rejection on the grounds that non of the above references teaches or suggests the screening of gene products that are differentially expressed upon infection for the ability to induce a specific immune response. The examiner finds this argument persuasive as the prior art is devoid of any teaching or suggestion of a host cell gene product that is up-regulated upon infection *and* immunogenic. In the absence of a suggestion that such a gene product exists, there is no reasonable expectation of success in combining the teachings of the prior art to achieve the claimed method.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
February 18, 2003

JAMES HOUSEL 2/23/03
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